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COBALT⁶⁰ BEAM THERAPY — COMMENTS, HOPES AND AIMS*

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This is an auspicious occasion in the life of Canadian Medicine. A peacetime "beehive" of atomic energy has been duly controlled and placed in Victoria Hospital, London, Ontario. It is a pretentious weapon designated for the destruction of life's fifth column — cancer, and to the end that human cells once living in peace and harmony, may again resume their normal functions.

By brilliant painstaking perseverance a most modest, genial group of young physicists and engineers of the National Research Council and the Eldorado Mining and Refining (1944) Limited, have ingeniously created the Cobalt⁶⁰ Beam Therapy Unit, and it would be remiss were I to pass over this opportunity of extending, on behalf of the medical fraternity throughout the world, our most grateful thanks to these young Canadian scientists.

I wish also, on behalf of the Victoria Hospital Board of Trustees and the University of Western Ontario Medical Staff associated with our work, to express our deep indebtedness to The Ontario Cancer Foundation and the Federal Department of Health, for making available to this city the world's first commercial massive Cobalt⁶⁰ Beam Unit.

What was being activated in the Chalk River pile over the twelve months' period alongside our Cobalt, I do not know, less do I care, for implicitly I trust Canadian scientists and physicians to bend their last efforts toward achievements for the betterment of humanity and in the final interest of peace. It is sufficient to know that the spear has been turned into the ploughshare, and in our hands has been placed an anti-cancer weapon, powerful in its output, deep in its penetration.

Cobalt⁶⁰ epitomizes the aspirations of both physicists and radiologists who, since 1896 when x-rays were first used as a thera-

peutic agent, have striven to acquire improvement in *quality* and *quantity* of rays. By steadily increasing voltage, skin treatment distance and filtration over these fifty years, progress to this end has been made. Paralleling these physical developments toward perfection in x-ray therapeutic apparatus, has been the expansion of radium technique with new dosage systems and bigger bombs. Isotopes appeared, research progressed until came 1951 when Cobalt⁶⁰ raised its mighty head to fulfil all dreams of gamma ray *quantity*. Furthermore by the specificity of Cobalt's two destructive, short, penetrating wave lengths, we are offered a unique advance in *quality*: hence, a new tool becomes available to extend our observations on the true biological importance of these persistently sought-after improvements in physical factors.

We ask ourselves and propose, along with others, to seek the answers to such questions as these:

- (1) Are the heretofore radio-resistant tumours more sensitive to this new beam?
- (2) Are normal tissues surrounding cancer less sensitive? That is, do they withstand a higher quality shorter wave length better than the longer heterogeneous wave lengths of radium bombs, and moderate x-ray voltage?
- (3) Is the biological effect of irradiation independent of wave length?

To arrive at case selection for bomb treatment requires stock-taking of cancer control effectiveness today. The necessity for earnest concentrated work is established through Dr. Sellers' Ontario Statistical Report of 1949¹, in which cancer deaths are shown to have increased from 3524, or 9.2 per cent in 1929, to 6209, or 14.7 per cent in 1948. That no panic is warranted is supported from the same report which shows that when the figures are corrected for sex and age, the cancer death rate has not appreciably altered since 1936.

*Presented at installation ceremonies, November 12, 1951, Victoria Hospital, London, Ontario.

Laymen and physicians emphatically have shown they will tolerate nothing short of a downward trend in this cancer mortality rate, and to this end the Canadian Medical Association, the Canadian Cancer Society, the National Cancer Institute and such provincial cancer control bodies, as the Ontario Cancer Foundation, are pooling their education, research, and service efforts against this neoplastic rascal. The Cobalt⁶⁰ Bomb is one tangible expression of this pooled effectiveness.

I would remind you of another expression, less tangible, of the vast numbers of cured cancer folk who just go along housekeeping or do a bit of fishing, but who have applied to themselves the good wisdom of early diagnosis and have nicely evaded the statistician. Morbid curiosity seems more concerned about the many people who die than about the beautiful, healthy, happy ways in which they live. Can any country in the world tell us how many cancer victims lived in 1949? Or in 1950? No, they can not, but shortly they can tell us how many have died. The 1951 Statistical Survey of Uterine Cervix Cancer² cases from our own clinic, reported to Professor Heyman of Stockholm, reveals that 96 per cent of Stage 1, or early cases were cured.

The cardinal deduction from these observations is that we must be relentless in preaching the doctrine of early diagnosis and continue with precision the application throughout this country of tried and accepted methods.

But there is a malicious cancer group that continues to defy us. I refer, as examples, to cancer of the lung, the gullet, the pancreas and the upper end of the stomach. These lesions are so insidious in their onset, so close to vital structures, so lethal in their effect that immediately and without delay we must bring to bear upon them the full potentialities of Cobalt⁶⁰ Beam Therapy.

Already we are utilising exact localization of tumour, and ultra precision in applying Cobalt gamma rays by Manchester beam direction technique. Without precision from the beginning we will learn little and accomplish less. Very shortly the rotation table, or the so-called "merry-go-round" method of treatment should be available for trial.

Then there is the group so curable by acceptable means when seen early, but oftentimes late in presenting themselves for treatment, such as the uterus, breast, rectum or ovary upon which we propose to focus this method.

Indeed, ladies and gentlemen, it is only right that you should ask what and how many we expect to cure with this bomb. It is only wrong at this early date that I should have the answers. Be assured the Bomb will materially expand the effectiveness of radiotherapy in the control of cancer. Be assured from the humanitarian standpoint we will let no opportunity pass to evaluate its clinical or palliative influence on someone's cancer out of control where life to the patient still seems sweet: for the words of Lord Tennyson still hold,

*"No life that breathes with human breath
Has ever truly longed for death.
Tis life, not death, for which we pant,
Abundant life is what we want."*

Shortly we will know Cobalt's limitations, but years will be required to accurately assess the true anti-cancer position of this most valuable weapon, Cobalt⁶⁰ Beam Therapy, the radiotherapeutic gem of 1951.

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Sponsored by: The British Empire Cancer Campaign, London, The Donner Foundation, Philadelphia; The Cancerforeningen, Stockholm; The World Health Organization.

Our congratulations are extended to eight of our members who received their Fellowship in the Royal College of Physicians and Surgeons of Canada this past fall:

Dr. Origène Dufresne, Montreal
Dr. Jules Gosselin, Québec
Dr. Albert Jutras, Montreal
Dr. J. W. McKay, Montreal

Dr. Carleton B. Peirce, Montreal
Dr. A. C. Singleton, Toronto
Dr. Digby Wheeler, Winnipeg
Dr. H. M. Worth, Vancouver.

HENOCH'S PURPURA: *

Its Radiological Diagnosis

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Non-thrombocytopenic or "Allergic" Purpura may assume a wide variety of clinical forms. One of the most confusing is that first described by the great German pediatrician Edouard Henoch¹, (1820-1910) who reported his first case, a boy of 15, in 1868. Six years later, he presented this with three more cases (aged 3, 5 and 13 respectively), as a distinct clinical entity: "Characteristic for all is the combination of purpura and the striking intestinal symptoms which are present in the form of colic, tenderness of the abdomen, vomiting, and in haemorrhages, rheumatoid pains and swelling. Characteristic furthermore is the appearance of these symptoms in attacks with an interval of eight days or more, so that in the usual cases, 3 to 7 weeks pass before the process clears up; in the last case, indeed, more than 3 months." He adds: "The fever was always quite moderate, sometimes entirely absent." All his cases recovered, and of the first he notes: "Concerning the therapy used at that time, I know only that preparations of opium were the most efficient, while purgatives seemed to be harmful; the boy moreover became entirely healthy and developed into a strong young man." — a striking resemblance indeed to the case we shall report.

In these early cases, Henoch was not faced with the diagnostic problem which develops when the "striking intestinal symptoms" antedate the purpura by days or weeks. In this event, it is difficult to decide whether or not one is dealing with such an acute abdominal emergency as intussusception in a young child, or, in older persons, acute appendicitis, a ruptured viscus, or a mesenteric thrombosis. In such cases, roentgenology can be of assistance in the demonstration of changes in the mucosal pattern of the small intestine which, in conjunction with the clinical picture, may be reasonably distinctive.

Case Report — H.B. — a previously healthy farm boy of 16 was admitted to hospital 31 Aug. 1946, nine days after the sudden onset of malaise, gnawing epigastric distress, vomiting and obstinate constipation. From the beginning of his illness, lethargy had been marked, and he had taken little to eat or drink.

There had been periodic vomiting. In the two days before admission abdominal pain became more colicky and severe, and vomiting more pronounced. He had no spontaneous bowel evacuations, and two enemas in the 48 hours previous to coming to hospital had produced small, dark scybalae. For 24 hours, vomiting had been severe and "like coffee grounds".

While he was very ill on admission, the temperature was only 99° and never rose above this level during his entire illness. At first the abdomen was flat and relaxed with only mild epigastric tenderness. Red cell count was 4,000,000; haemoglobin 11.5 grams; white blood count 13,300 with 74% neutrophils. General examination was remarkably non-revealing. After adequate parenteral fluids, he did improve considerably, and for several days seemed to be getting better. An enema two days after admission produced a soft brown stool, with no signs of blood. Shortly thereafter, however, abdominal pain became severe and he started to vomit frequently. There was no change in the white count or temperature. Surgical consultations were held, and a tentative diagnosis of either duodenal ulcer or acute gastroenteritis was made.

A radiological study of the gastro-intestinal tract was made on 4 Sept. 46. (Figure 1.) The pyloric portion of the stomach and the duodenum were rather rigid, narrowed, and their silhouette irregular, inversely scalloped and notched. The mucous membrane pattern was abnormal or lost. There was stasis in the greater portion of the duodenum; the rest of the duodenum and a portion of the jejunum showed similar changes with less marked filling. This pattern was exactly re-duplicated on several films at this examination. This was reported at the time as due to an inflammatory lesion of the stomach, duodenum and jejunum.

Following this examination the boy became increasingly ill. After further consultations, on 6 Sept. 46, a sigmoidoscopic examination revealed a very congested rectal mucosa with a number of small haemorrhagic areas, several of which had apparently ulcerated. Considerable quantities of mucus were noted to be coming down from above. The clinical impression at this stage was that the patient had a diffuse infective gastro-enteritis. Several blood cultures were made with negative results. All agglutination tests were negative.

* Presented by Dr. W. A. Jones in part at the Mid-Winter Session of the Canadian Association of Radiologists 4 Jan. 47.

During the second week in hospital his condition became even more critical. He continued to show a low-grade fever of only one degree, but the pulse was quite fast and he appeared very toxic. He was still vomiting frequently and taking very little by mouth. By 17 Sept. 1946, abdominal pain was more generalized and severe, and as there was



Fig. 1 — 4 Sept. 46.

Thirteen days after the onset of acute gastrointestinal symptoms and 25 days before the appearance of purpura. Note the narrowed, rather rigid pyloric portion of the stomach and the duodenum with an irregular, inversely scalloped and notched silhouette of the abnormal mucous membrane pattern. The distal duodenum and a portion of the jejunum showed similar changes with less marked filling. This pattern remains fixed throughout the several films of this examination.

generalized rebound tenderness peritonitis was suspected. The white blood count had risen to 24,900. On that day at an exploratory laparotomy, the small bowel was found to be patchily thickened and oedematous from the pylorus to the terminal ileum. There was no peritonitis. A mesenteric lymph node removed for biopsy showed no special pathological features.

Post-operatively, the patient was placed on sulfathalidine. For a time he seemed to improve. Then, colicky abdominal pain became very troublesome and required large doses of opiates (morphine and HMC's).

With the exacerbation of abdominal symptoms, purpuric spots appeared for the first time, on 29 Sept. 46, 38 days after the first

symptoms of illness. The purpura was most obvious on the thighs, but appeared in successive crops over the entire lower extremities. Concomitantly, his general condition deteriorated rapidly. His haemoglobin dropped to 9 grams and his red count to 3,250,000. Platelet count, (done for the first time) was 1,062,000. Vomiting continued, frankly bloody, and the patient began passing soft stools with blood and mucus.

By October 6th, his condition was deemed critical and his life was indeed despaired of. A few days later, however, he began to improve rather rapidly, so that, by the end of October (Fig. 2), he had recovered from his

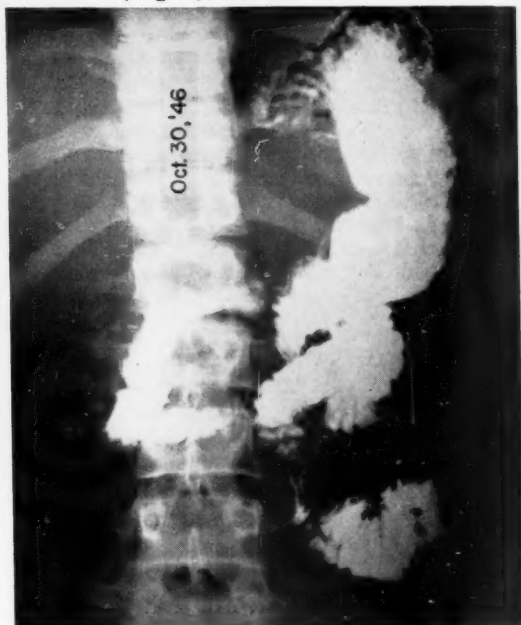


Fig. 2 — 30 Oct. 46.

Nearly two months after that of Fig. 1; about six weeks after the exploratory laparotomy and four weeks after appearance of purpura. Eating and drinking well. Much improved. Occasional crampy pain.

Stomach relatively normal. Still some duodenal stasis but the irregularity of contour is not as pronounced and the silhouette changes a little during the several films. The jejunum now fills widely, its mucosal pattern is coarse, with some stasis.

lethargic state and was eating and drinking well. He still had occasional episodes of very severe crampy abdominal pain, some of which were definitely provoked by dietary indiscretion when he broke the bland, low-residue regimen imposed upon him.

On November 7th, he was sent home — weight 120 lbs., eating well, having daily soft, formed stools, and requiring no opiates or other medication.

About the first of December, 14 weeks after the onset of his illness, he seemed to have a slight recurrence of purpura, his ankles became sore and swollen for a few days. His general health was unaffected and he continued to gain rapidly so that by December 15th, his weight was reported to be 150 lbs. (Fig. 3).



Fig. 3 — 30 Dec. 46.

Nearly four months after Fig. 1. Symptom free.

There is still some narrowing of the duodenal cap. The duodenal outline is still a little irregular but stasis is not as marked. The mucous membrane pattern of the jejunum remains a little coarse, but on the whole a remarkable degree of improvement is evident. Moreover, the pattern changes, and is not constantly reduplicated as in the first examination.

This patient has been followed periodically. (Fig. 4). He has had no recurrence and when last examined on 27 Dec. 50, he was an exceptionally robust and healthy young man of 20, 5 feet, 10 inches in height, weighing 180½ lbs. He had no gastro-intestinal complaints, was eating heartily and had one well-formed stool daily.

The illustrative skiagraphs cover the period from 4 Sept. 46, twenty-five days before the appearance of purpura to four years later.

The radiological appearance of the gastro-intestinal tract is now normal. (Fig. 5).

Oct. 21, '48

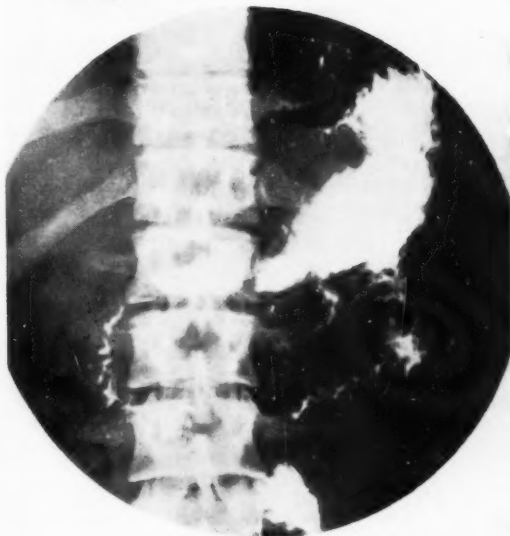


Fig. 4 — 21 Oct. 48.

Two years later. Symptom free.

The distal duodenum and the jejunum were poorly filled and presented a "ravelled string" appearance, constant in all the films, with some segmentation.

Dec. 27, '50



Fig. 5 — 27 Dec. 50.

Symptom free.

Stomach, duodenum and jejunum are now all apparently normal.

Whitmore and Peterson² reported a similar case in 1945. They discussed the diagnostic problem in detail and described the small intestine changes of alteration in the normal mucosal pattern, a tendency to stasis, and irregularity of the intestinal outline, resembling small diverticula and ulcers. Such would presumably result from haemorrhage into the mucosal layer, with obliteration of the normal mucosal pattern, separation of patches of mucosa and subsequent ulceration. Unfortunately for us, their article did not come to our attention until after our patient developed purpuric spots and no longer presented a diagnostic problem.

Kraemer³, in regard to another case with onset of watery diarrhoea and "lower abdominal cramp", stated: "I was able to confirm Whitmore and Peterson's description of the abnormal small bowel x-ray pattern in Henoch's Purpura. The patient's films showed segmentation of the barium in the ileum and a loss of normal rugal pattern in the jejunum. Films taken after subsidence of symptoms also showed a normal small bowel pattern." No skiagraphs were shown with this paper, but the author states: "A gastro-intestinal study showed excessive segmentation and irregular filling in the small bowel resembling the pattern usually associated with a vitamin deficiency." In his case the purpura was noted twenty-odd days after the onset, one or two days following x-ray examination.

Fetter and Mills⁴ described a case showing "duodenal spasm and irritability, constrictive obstruction, at the beginning of the third portion of the duodenum. Dilatation occurred proximal to this. After the duodenum distal to the site of obstruction was visualized, the mucosal pattern was shown to be distorted by widening and irregular filling of the mucosal folds. The entire small bowel was shown to have an irregular pattern." Three months later the duodenum and small bowel were reported negative. The x-ray examination of this patient was made more than three weeks after the onset of his symptoms and after the development of purpura.

Esposito⁵ presented two further cases in January, 1950. In one, admitted with generalized abdominal pain, nausea, vomiting and mild diarrhoea, "Loops of jejunum and ileum showed irregularity in the calibre of the lumen. Some segmentation was present. The margins of the contracted hypertonic loops showed considerable irregularity with a loss of mucosal architecture. In some areas the irregular mucosal outline was suggestive of ulceration. Impression — an acute inflammatory enteritis." Eleven days later (nineteen days after onset), a purpuric eruption was noted.

In the other, symptoms began with dull abdominal pain and slight distention of abdomen, no nausea, no vomiting. Eight days after the onset of the condition, and following improvement in the abdominal symptoms, but with occult blood present in the stool, the x-ray examination revealed "the distal portion of the duodenum and loops of jejunum showed markedly widened oedematous mucosal folds. Deep and irregular mucosal outlines were observed. There were two dilated segmented ileal loops. These findings were interpreted as indicating an enteritis."

Eleven days from the onset he developed purpura. About six weeks later the x-ray examination revealed "A slight tendency to coarsening of the mucosal outlines of small intestinal loops with slight segmentation, probably indicating some residual disturbance in physiology."

Discussion:

In comparison with these reports, it will be seen that in our patient the radiological appearance of the gastro-intestinal system did not revert to normal, as in these other reported cases.

It is perhaps difficult to assess, on the roentgenograms, just how much of the rather bizarre pattern may be due to ulceration and how much is caused by disordered motor function. It is felt, however, that the appearance presented in the primary examination on 4 Sept. 46, was that of ulceration and inflammation. What followed (Figs. 2 to 5) is debatable.

Up to a period of two years, following the acute symptoms, we did not find a normal looking pattern in our patient. There might, of course, have been times in between the x-ray examinations when the pattern would have been found normal if the patient had been studied radiologically.

Summary:

Our case is presented as another example of the difficulties in the early clinical diagnosis of this type of purpura. It illustrates the information which the radiologic examination can give, and which should afford a clue to the correct diagnosis, thus possibly avoiding a dangerous exploratory operation.

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THE BETATRON IN CANCER THERAPY

Part I

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The betatron, developed by Kerst,^{12, 13, 14} is an instrument which produces electrons or x-rays of very high energy, without the use of correspondingly high voltages. In the summer of 1948, a 25 Mev. betatron was installed at the Physics Department of the University of Saskatchewan. The instrument itself was purchased by the Canadian Atomic Energy Control Board, and the building which houses it was constructed by the Saskatchewan Provincial Government. Following a period of about nine months during which numerous physical investigations of the machine were made, the actual treatment of certain selected advanced cases of malignant disease was started in March of 1949. Prior to this time, only one patient had been treated with high energy x-rays of the order of 22 Mev.²⁰ Although only little more than two years have elapsed since the start of these experiments, it is thought worthwhile recording clinical experience with the machine at this time, since several centres will probably be using it in the near future, and there is no guidance in the literature concerning the therapeutic use of x-rays of energies above 2 Mev.

Biological Effect

Quastler²⁵ and his associates have published the only information available on the biological effects of these x-rays. Quantitatively they are different from 200 K.V. x-rays. This difference appears to vary, depending upon the type of biological material used, but in all experiments, high energy x-rays have been less efficient in producing any given change. It was found that the biological effectiveness of 20 Mev. x-rays for acute death in mice²¹, compared with 200 K.V. x-rays, was 79%, for the graying of the coat of mice¹, 72%, and for the mutagenic effects in *Drosophila Melanogaster*, 70%¹⁸.

In all these experiments comparisons of dosage were made by the use of Victoreen thimble chamber. For absolute comparative measurements of ionization, this method is certainly open to criticism. However, later experiments²³ have shown that there are definite quantitative differences in the production of different biological changes when 20 Mev. x-rays are compared with 200 K.V. x-rays. A lack of biological uniformity has also been well proven in the case of neutrons^{2, 19, 20, 29, 35}.

The biological effects of radiations are undoubtedly caused by ionization in the tissues. The method of production of the ionization is different, although in each case it is finally brought about by the setting in motion of electrons, and for this reason, one would not expect there to be any biological difference in the effect of 200 K.V. x-rays and 20 Mev. x-rays. At 20 K.V. most of the ionization is produced by the Compton effect (very little by photo-electric absorption). At 20 Mev., however, ionization is produced by the Compton electrons and electron pairs about equally.

Probably different biological changes are a function of the spatial distribution of the ions^{17, 5}. Gray⁶ has given comparisons of the ions produced per micron of tissue for various radiations. He shows that for 20-30 million volt x-rays the mean linear ion density is 8.5, compared with 11 for radium gamma rays, 80 for 200 K.V. x-rays, and 290-1,100 for neutrons. The minimum possible calculated figure is 6.3. It is possible that this variation of differential ionization may be of therapeutic value²⁸.

Stone³³ has solemnly warned against the use of high energy radiations in the treatment of human material, until a great deal of biological experimentation has been carried out. His conclusions, however, were drawn from experience with particulate radiation (neutrons), which produces a very high linear ion density, depending to some extent on the speed of the neutrons. It is not thought that such dangers exist in the use of high energy x-rays of the order 20 - 25 Mev. since the linear ion density is quite close to that of radium gamma rays. Further there is evidence to show that the induced radioactivity produced by irradiation of tissues with 22 Mev. x-rays, account for only about 0.01% of the total ionization produced²². Neutrons in the primary beam account for only 0.001% of the ionization¹¹. This is considered negligible.

General Considerations

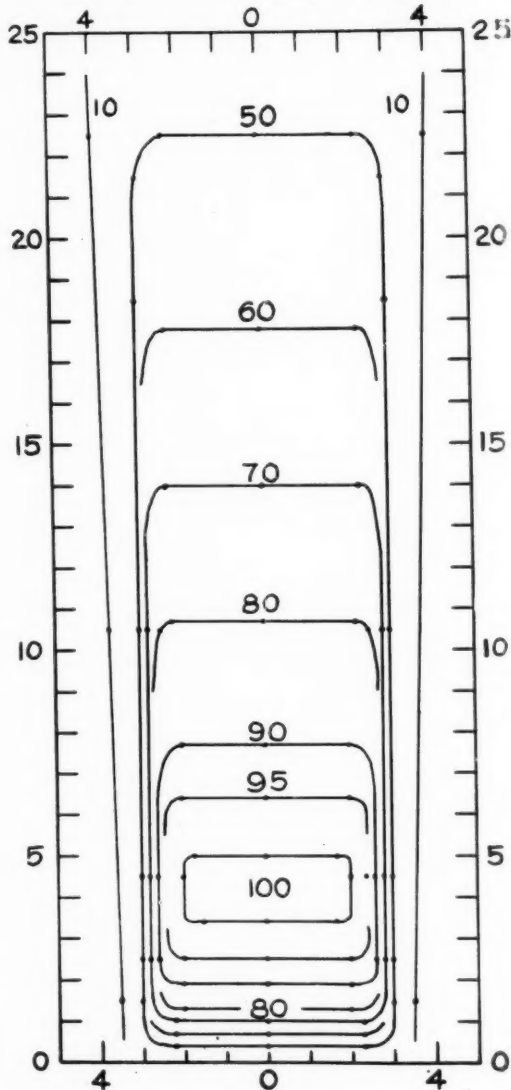
The betatron at the University of Saskatchewan is housed in a special low lying building. The fixed beam is below the ground level so that the rays which pass through the walls of the building are absorbed finally in the earth. (A detailed description of the building may be found elsewhere⁷.) Almost

all the x-rays from the betatron are in the main beam, but a considerable amount of lead shielding is required on all sides of the main beam. Any field up to a 15 x 10 cms. rectangle at a focal skin distance of 105 cms. can be obtained. If larger fields are required, the F.S.D. must be increased. The fields are delineated by the insertion of various sizes of hollow lead plugs. Cones of thin metal are used to aid in positioning of patients. The ends of the cones are closed with thin slabs of balsa wood, which is equivalent in thickness to 0.8 millimeters of tissue. The ends are closed so that the cones can be used for compression when necessary.

The beam is fixed in a horizontal position. On the wall of the room, opposite to the machine, a back-pointing collimator²¹ is used so that the exit point in the centre of the beam is clearly marked on the patient's skin. A special platform twenty-one inches high has to be used since the beam is five feet above the surface of the floor. If this point had been considered before the installation of the machine, it could have been installed at a lower level. An ordinary tilting treatment couch has been used for all treatments, but it has been found by experience that lateral tilting of the patient, except to 90°, is most unsatisfactory and is indeed usually unnecessary. The isodose curves are such that very simple layouts are possible. The betatron is separated from the control room by a two-foot concrete wall. The patient is viewed during treatment by means of a mirror arrangement. The radiation received by the staff is well below the tolerance levels.

One of the main attractions in the application of betatron to radiotherapy is the distribution of dosage obtained in the tissues. With conventional x-rays, the dose is in general at a maximum at the skin surface and becomes less thereafter. With 22 Mev. x-rays, however, the somewhat anomalous result is obtained, that the maximum dose falls at a depth between 3 and 5 cms. whereas the surface of the skin received almost nothing. If a Victoreen chamber is placed in an x-ray beam of this kind, in air, practically no reading will be obtained. A maximum reading is obtained when the chamber is surrounded with material 4 cms. thick. Isodose curves obtained from the betatron^{3, 16} show a pointed appearance indicating that the dose in the centre of the field is very high but falls off rapidly towards the sides. This renders the unfiltered beam unsuitable for radiation therapy, as homogeneity of the beam, from side to side, is desirable¹. Johns has developed a copper compensating filter which flattens the isodose surfaces and thus render radiation thera-

py practicable². This mechanism does not act as a filter in the ordinary sense, as the quality of the radiation is unchanged. (Fig. 1.)



From a physical point of view, the betatron offers considerable advantages in treatment of deep-seated lesions. The surface dose is small whereas a very high depth dose can be obtained. There is very little scatter outside the beam since almost all the electrons are scattered in a forward direction and hence differences in the field size make a negligible difference to the output and depth dose.

X-rays of this energy produce almost the same ionization whatever tissue is traversed. Hence there should not be the same tendency

to bone or cartilage necrosis as with ordinary therapeutic x-rays, although there may be a small differential effect¹⁰. Furthermore, bone marrow will receive nearly the same dose as surrounding tissues, whereas with conventional x-rays it receives a considerably higher dose than other tissues, because of its surrounding bone. This has been admirably demonstrated by Spiers³⁰.

It has been further shown that, when using 22 Mev. x-rays, the integral dose, received when a given volume of tissue inside the body is raised to a certain dose, is in general less than one half that received when x-rays of 400 K.V. are used⁸.

It is rather interesting, but not of major importance, to note that the exit dose in a patient is always larger than the entrance dose.

During operation, the betatron produces a loud whining noise of the order of 92 decibels⁷. All rooms are soundproofed and in the control room the intensity is only 54 decibels. The noise of the machine in operation does not appear to disturb the patients once they have been warned. It has not been necessary to use ear plugs.

The machine has been operated at between 22 and 23 Mev. The output, using the compensating filter is between 50 and 100 equivalent roentgens per minute at a focal skin distance of 105 cms. Since the output of the machine varies erratically with changes in injection and contraction timing, a monitoring device of the integrating iometer type is used, and the machine is set to deliver the predetermined dose¹¹. An automatic device shuts the machine off when this dose is delivered.

Factors Used in the Treatment of Patients

Although the betatron will operate at voltages of 25 - 28 Mev., all patients so far have been treated with either 22 or 23 Mev. x-rays. The focal skin distance has been 105 cms. From a point of view of depth dose, there is virtually no advantage in increasing the focal skin distance, since about the only effect attained would be an increase in the exit dose. A decrease in focal skin distance would only be practical for small fields.

Since the surface dose is very small (about 15%), a prescription in terms of the surface dose would not convey a great deal of meaning. We have, therefore, adopted the convention of stating as the given dose the maximum dose received at 4 cms. deep—that is, at the 100% level. When fields are used on any part of the body, the exit dose on the

other side will be greater than the entrance dose. It is difficult to state the actual skin dose at a point of entrance since the dose at the surface (15%) rises to 100% at approximately 3 cms. depth¹¹. In the first few millimeters, the percentage depth dose rises very rapidly and it is obvious that the surface dose of radiation cannot have any biological effect because the surface layer of the skin is dead keratinized tissue. An arbitrary depth of 4 mms. is suggested by Klumppar¹⁵ as the critical point at which biological changes in the skin originate. Strandquist,^{31, 32} on the other hand, states this point to be 3 mms. deep. This is an artificial convention and of doubtful value. We have adopted a figure 40% as representing an approximate effective entrance skin dose.

A confirmatory finding, during the treatment of patients, is that the effective incident skin dose is considerably less than 50% of the maximum. Using a single field on the anterior chest, as was done in one case, the exit area developed an erythema followed by marked pigmentation. The entrance field showed no erythema, but a subsequent slight pigmentation appeared. Using this convention, the stated surface dose was 40%, compared with an exit dose of 51%. Thus the entrance dose must be significantly below 51%.

Selection of Cases

Since clinical work was started with the betatron, approximately 75 patients suffering from advanced malignant disease have been treated. These patients were chosen because it was not considered that conventional treatment of any kind would offer more than the most temporary palliation. Many were recurrent, following surgery or radiation treatment, or were found inoperable on surgical exploration.

In all patients, pathological proof of malignancy was obtained before treatment was started.

The first 61 patients were treated over a period of three weeks (approximately nineteen days) in an effort to establish therapeutic dosage levels for this over-all period. They were treated five times a week, usually each field daily. The remaining patients were treated five times a week over a period of five weeks (approximately thirty-three days) and using, of course, somewhat higher dosage. It was not always possible to deliver the planned dose in exactly these times, owing to occasional break-downs of the machine, and other factors, such as reactions of the patients.

Of the 75 patients treated, the last 9 are omitted from the subsequent discussion as their treatment is too recent for any conclusion to be drawn. Eight other patients are excluded because their treatment was not completed. Of these cases, one patient was treated by a combined method; in another, the treatment was abandoned because the machine broke down after the first treatment; in 5 patients, the general condition was so poor that treatment was abandoned after one to five treatments; in the final case, treatment was discontinued after five exposures as the patient suffered an accidental fracture of the neck of the femur. These omissions leave a total of 58 patients for consideration. At the present time, 26 of these people are alive and 32 are dead. Since the patients chosen were all very advanced patients, and sometimes almost terminal, this record should not hastily be judged poor. If one of these patients survives five years, we will be well satisfied.

Reactions

1. Constitutional

Large volumes in the pelvis and chest were treated in most patients. No patient, however, developed radiation sickness, bearing out the physical calculation of a lower integral dose for a given dose to a volume, compared with conventional x-rays. In all patients weekly blood counts, including differential white counts and platelet counts, were made. In no patient did the white count fall below 3,000 cells per cu. mm., and usually it was unaffected. No significant change in the red cell count, haemoglobin level or platelet count was found.

2. Local Tissue

The local tissue reactions were found to be the limiting factor in dosage. Towards the end of treatment to the pelvis (virtually the whole pelvis was irradiated in each case) diarrhoea and or urinary frequency usually developed and in some patients was sufficiently severe to force termination of the treatment.

When large volumes of the chest were irradiated, the limiting factor was often the reaction inside the oesophagus, characterized by dysphagia or increasing pain on swallowing.

3. Skin

Most patients showed no erythema. A few patients developed a mild erythema with a skin dose as low as 2000r in three weeks, but usually erythema did not develop in patients receiving less than 3000r in three weeks. All these figures refer to large fields.

Prior to these experiments, x-rays of voltages higher than two million had not been used systematically on human patients. In view, therefore, of Stone's³⁴ experience with neutrons, these high energy x-rays were approached with trepidation. It was necessary to establish that no reactions foreign to those accompanying the use of ordinary x-rays would occur, and that no deleterious side effects would be produced. Dosage levels were unknown. It is incorrect to use the term "roentgen" in the description of dosage in this paper but it is a convenient term, although not strictly comparable with "roentgens" of ordinary x-rays. The 22 Mev. roentgen is considerably less efficient biologically than the 200 K.V. roentgen, and hence much larger doses should be used.

With these thoughts in mind, the first patient, who was suffering from a post-operative recurrence of carcinoma of the rectum, was treated to a low tumor dose of 3000r. There were no skin and constitutional reactions and no effect on the tumor. Doses were then steadily raised with subsequent patients until tolerance levels were established. It was important to confine the over-all treatment time to the same figure in each patient so that these comparative levels could be more quickly arrived at. An over-all time of three weeks was chosen originally. After 61 cases had been treated, the over-all time was raised to five weeks.

In spite of the large fields used, the tolerance levels were not limited by either the constitutional effect of the radiation or the skin reaction. The dosage was limited by the local reaction of the tissues in the irradiation field. Thus, when the pelvis was being irradiated, it was the diarrhoea and tenesmus secondary to the effect on the bowel which limited the dose which the tumor could be given. In patients with carcinoma of the lung, mediastinum or oesophagus, it was the dysphagia caused by the inclusion of the oesophagus in the irradiated zone which limited the dose. In patients with pelvic carcinoma a dose of 6000 roentgens, and in patients of thoracic carcinoma a dose of 6,500 roentgens, (as determined by the Victoreen r meter), given in an overall time of three weeks, was found the maximum which the tissues could tolerate. Even with this dose the reactions occasionally were so severe that hospital care with intravenous feedings were necessary to tide the patient over the reaction phase.

This dosage level was found, in a majority of patients, to cause disappearance of the tumor. Unfortunately, however, there was often a local recurrence indicating a failure

of treatment from inadequate dosage. With this in mind, the over-all time was increased to five weeks and the tumor dose increased to 7,500 roentgens. Again the limiting factor has been the local tissue reaction. Too little time has yet elapsed to say whether the tumor lethal effect has been enhanced by this change. As neurological tissue tolerates radiation less well than other tissues, ^{27, 34}, a dose approximately four-fifths that given for carcinomata of the lung or pelvis was adopted as probably within the safety limits. Thus with the three-week course of treatment, a dose of 5500 roentgens, and with the five-week course a dose of 6000 roentgens, has been used.

(Editor's Note: Conclusion of this paper will appear in the following issue (March) of the JCAR.)

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BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

The Normal Cerebral Angiogram, by Arthur Ecker, M.D., Ph.D. (Neurology). Charles C. Thomas, Springfield, Illinois.

Roentgen Anatomy, by David Steel, M.D., Charles C. Thomas, Springfield, Illinois.

DIAPHRAGMATIC HERNIA *

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Herniation of the abdominal viscera through rupture or an enlarged hiatus of the diaphragm is not as infrequent as is generally believed. In fact, numerous cases have been reported by different authors; and, in all probability, many more could have been reported if not overlooked by all of us in the course of our radiological practice.

During the early months of 1950, we were fortunate enough to encounter a series of six consecutive cases. With the exception of one which had been suspected clinically, all the other cases were incidental radiological findings disclosed by roentgenograms of the chest or abdomen without contrast media.

Indeed, there is nothing surprising about that, for it is well known that, clinically, such herniae are rarely diagnosed, even after attentive observation and methodical examination. Even so, we believe that diagnosis at a glance on routine X-rays films would be rather exceptional: the abnormal shadows produced by hernia over the diaphragmatic region could be easily overlooked were the films not carefully scrutinized.

We believe also that close cooperation should exist between clinician and radiologist. Informative discussions relative to extraneous shadows observed on "flat plates" would emphasize the necessity for more frequent roentgen exploration with contrast media, to confirm or disprove the presence of a suspected hernia.

Etiology:

Etiological factors may be: Congenital, acquired and traumatic. The diaphragm being formed by semi-united and multiple fasciculi, two anterior, two posterior and two lateral, has definite points of weakness which may eventually become the site of a hernia. A common point of weakness lies in the foramen of Morgagni. Posteriorly, the foramen of Bochdalek and the oesophageal, aortic and caval hiati are all favorite sites for the occurrence of hernia. Upon inspiration the positive pressure within the abdominal cavity, increased by cough, direct or indirect injury, parturition, new growths, will favor hernia formation. Penetrating wounds, (surgical or otherwise), or sub-diaphragmatic abscess commu-

nicating by a fistulous opening into the thoracic cavity may also predispose to hernia. Hernia is more common on the left side than the right. It may be found, however, in the mediastinal area, as well as on the right side. The liver may not always serve as a buffer to the right side of the diaphragm, and this should be kept in mind when considering diaphragmatic hernia. Any one of the abdominal organs occupying the sub-diaphragmatic region may possibly migrate through a breach in the diaphragm; the stomach, spleen, colon, small intestine, part of the liver, have all been found in one or another form of diaphragmatic hernia.

Symptoms and Clinical Signs:

The clinical recognition of diaphragmatic hernia from the subjective symptoms alone is often very difficult, and only the roentgen ray examination can be depended on to clear up the diagnosis. Upon exhaustive study of the clinical case histories of the six patients whose x-rays showed hernia, in five there were no symptoms suggestive of this condition. There is little doubt that the clinical complaints are usually attributed to some trouble of one of the intra-thoracic or intra-abdominal viscera. Various degrees of pain in the region of the stomach, eructation, vomiting and or anorexia may dominate the picture, and draw one's attention to trouble in the upper digestive tract.

Symptoms of diaphragmatic hernia are often so bizarre that palpitation, fainting spells and precordial distress may be attributed to a heart condition, whereas hernia into the posterior mediastinum, the real cause, will be overlooked. Loss of weight and anorexia are generally reported by the patient, but these have no real significance, and could very easily be caused by a variety of other pathological entities. One of our patients complained of "gas noises" in her chest.

Subjective symptoms of diaphragmatic hernia may be totally lacking; or they may be so mild that little does the patient suspect that his stomach is not just where it should be or that his colon has intruded into a region where his heart alone belongs.

Certain respiratory disturbances, such as cough, dyspnoea and polypnoea, are no more typical of diaphragmatic hernia than they would be for the majority of respiratory dis-

* Condensation of a paper presented at the 20th Congress of L'Association des Médecins de Langue Française du Canada, Montreal, September 1950.

ease. The cough associated with diaphragmatic hernia, however, is peculiar, and if reported by the patient may be suggestive. It comes on in paroxysms, is non-productive, has a tendency to exhaust the patient by increasing the intra-thoracic and intra-mediastinal pressure. Others complain of hiccough.

Physical signs are also very deceptive. Cyanosis, for example, occurring soon after birth, is so often a manifestation of some other congenital disease that it is practically impossible to impute to this sign the existence of diaphragmatic hernia. Crying spells or refusal to take food are of little help, even when these coincide with a retracted and poorly developed abdomen. One other of our patients had a slight ecchymosis which we attributed to a muscular tear in the epigastric region. Abdominal palpation is for the most part non-informative; but, on the contrary, chest signs may be more revealing and are therefore worthy of note:

- a) On percussion, in hernia on the left side, dextrocardia is always present in some degree.
- b) Heart sounds may be clearer on the right.
- c) There may be an entire absence of breath-sounds on the affected side.
- d) On auscultation there is a mixture of sounds such as gurgling, suggestive of peristalsis.
- e) The physical signs will vary with the amount of food, water or air in the stomach and bowel.

The temperature of the patient remains normal, even with pulmonary signs which could be attributed to a pneumothorax or to an acute involvement of lungs or pleura. Naturally, routine laboratory investigation will give no clue to the existing condition.

Radiological Diagnosis:

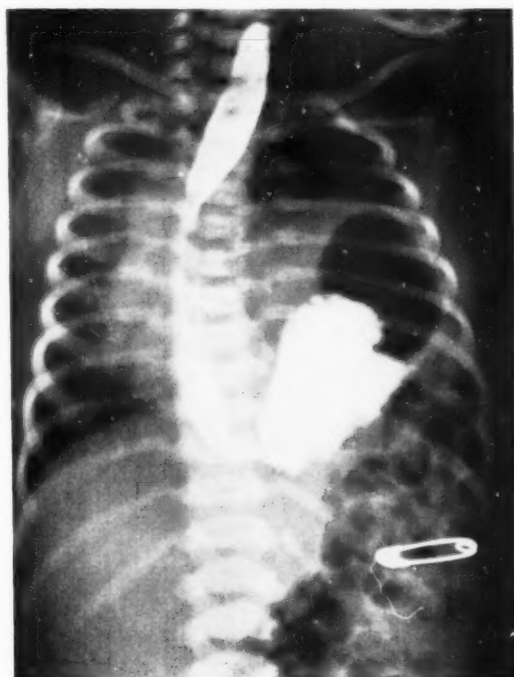
Most of the time, the presumptive diagnosis should be made on direct chest films in A.P. and lateral. Some atypical shadows will be apparent in a lung field or the mediastinum. At times there may be an area of irregular opacity at the base of one lung or occupying the whole of an hemithorax and not concordant with the clinical findings. Translucent areas with or without fluid levels are sometimes visible, and compare with the intestinal or gastric morphology. Retrosternal gas pockets are a striking feature. These shadows may be totally modified in their disposition from one film to another. The contour of the diaphragmatic dome may be obscured on one side. A dense circular shadow

may be superimposed upon the heart shadow, and caused by the wall of the herniated upper portion of the stomach. The heart appears displaced to the side opposite the hernia.

It is quite evident that, in the presence of presumptive signs, or in case of doubt, there is an indication to proceed with more enlightening x-ray exploration and visualize the suspected herniated organs with contrast media, care being taken to use the necessary positions which will demonstrate the hernia.

No mention will be made here of diaphragmatic eventration, in which no breach occurs in the diaphragm.

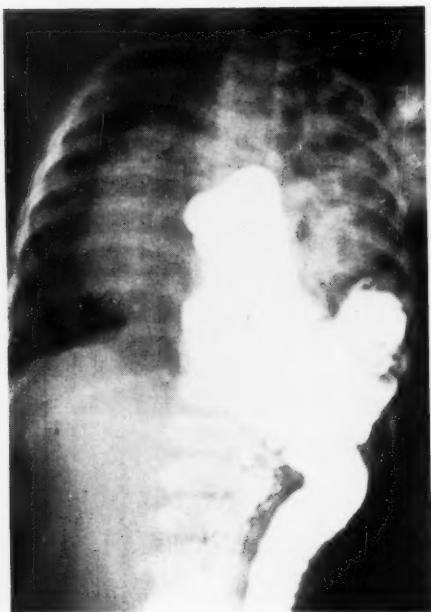
CASE REPORTS



Case No. 1: — Radiograph No. 1

Male infant, aged two days. Admitted to the Hospital on February 19, 1950, for cyanosis. Heart sounds heard on the right. Entire absence of breath-sounds on the left. Provisional clinical diagnosis: pneumothorax. The chest film was suggestive of diaphragmatic hernia on the left side, with gas shadows which appeared to be in the stomach and colon, filling the left thorax. The diaphragmatic contour was lost, and the heart shadow displaced into the right chest. A barium meal confirmed the presence of the stomach and part of the colon in the chest.

At operation, the surgeon found that the hernial sac contained the entire stomach, the left lobe of the liver and a considerable portion of colon. Post-operatively the patient suffered a left pneumothorax, which absorbed in three weeks. The final radiograph shows a normal thorax, with only a slight deformity of the left diaphragmatic dome. Patient was discharged from the Hospital cured, and there have been no untoward complications.



Case No. 2: — Radiograph No. 2

Female child, three months old, admitted to the Hospital in the early part of June, 1950, for dyspnoea and polypnoea.

There was no history of digestive disturbances, but she became cyanotic and distressed, particularly after feeding, and often suffered with hiccoughs. These symptoms had been noted by her parents soon after birth, and had become progressively worse.

A film of the chest on the 7th of June, revealed a large hernia through the left diaphragm evidenced by some intestinal gas shadows filling the left hemithorax. The diaphragmatic contour was abolished. The heart and mediastinum were displaced towards the right side of the chest. A barium meal showed that the stomach was not herniated, but the barium enema delineated the herniated colon. The remaining gas pattern was interpreted as pertaining to the small intestine.

On June 10th, the operation revealed a hernia of the posterior type, through the foramen of Bochdalek. The descending colon, about two-thirds of the transverse colon and almost the whole of the ileum had migrated into the left chest through a large breach.

A control film of the chest made on June 20th, (not illustrated here), showed a pneumothorax in the process of resorption, and the left lung semi-inflated. The child made an uneventful recovery; and is now in good shape.



Case No. 3: — Radiograph No. 3

Female, aged 56, admitted to the Hospital in February, 1950, complaining of weakness, vague digestive disturbances, of about three months' duration. She had pain in the upper abdomen, anorexia, with loss of strength and capacity to work. Pains were more severe after eating, and she complained of almost continual gas distention and eructation. There was no history of respiratory disturbances. Physical examination was negative, for the most part, except for a vague tenderness over the epigastric region and on auscultation, loud rales or gurgling sounds suggestive of peristalsis.

The x-ray examination of her stomach demonstrated a herniation of part of the greater tuberosity of the stomach through the oesophageal hiatus and appearing well over the

diaphragmatic contour. The barium was temporarily delayed at that level, and the filled oesophagus appeared displaced to the right, around the herniated portion of the stomach.

The patient was operated on, a few days later, and left the hospital cured.



Case No. 4: — Radiograph No. 4

Female, aged 63, admitted to the Hospital on March 27th, 1950, with a persistent cough. There was a history of heart trouble and hypertension; a cholecystectomy for lithiasis had been performed a few years before. She volunteered the information that, for the previous fifteen days, five children with whooping-cough had been under her supervision. She then began to cough herself, and her physician advised hospitalization, as there was no relief from the persistent cough. Nothing special was noted on physical examination except a small ecchymosis in the epigastric region, like a bruise. This might have been caused during the completion of the herniation, but was not attributed to same at the time. A chest film was requested, and showed a large condensation area involving and obscuring the right lower lung, through which some clear zones over fluid levels were in evidence. These findings did not coincide with the clinical findings of her family doctor, and control films were suggested. A.P. and lateral films taken the next day showed the same condensed area at the right base

with some clear zones, but the fluid levels had disappeared. The lateral film gave the clue to the problem by revealing the presence of gas patterns apparently pertaining to the colon, and passing from the anterior abdomen up to the retrosternal region and down to the base of the chest.

The barium enema confirmed our belief, and demonstrated the hernia of the colon through the anterior foramen. The whole transverse colon and part of the ascending colon had migrated to the retro-sternal region. Part of it was coiled in the right lower part of the chest. The enema was stopped there to avoid complications.

On going over the previous cholecystographic films taken two years before, it was noted that the hernia had not existed at that time.

Patient's recovery was uneventful, following cure of her hernia.

The bibliography on this type of hernia will be found in *Le Journal de Radiologie*, 1948, in an interesting article by Joubert de Beaujeu and R. Didier, in which 23 cases have been collected from the literature, and one published by them. Another case was published by H. Guillem (*Journal de Radiologie*, 1950, 5-6).



Case No. 5: — Radiograph No. 5

Female, aged 37, scoliotic, had undergone a partial gastrectomy in 1945 for gastric ulcer.

Her post-operative recovery had been normal; and she remained fairly well until October, 1949, when she complained of a sharp pain while walking on the street. This pain was localized in the upper left quadrant, and she began to vomit. The pain persisted, and she informed us that she had vomited after every meal. When admitted to the Hospital for x-ray, she was unable to retain the barium meal, which had to be administered through a Miller Abbott tube. This showed a hernia that had "exploded" through the oesophageal hiatus. It contained about half of the remaining part of the stomach, presenting a bizarre mushroom appearance, which we called the "atomic bomb".

Surgical repair resolved her problem, and she has been well since.



Case No. 6: — Radiograph No. 6

Female, aged, 48, had undergone a cholecystectomy ten days previously for gall stones. She now complained of dysphagia. Referred to us for examination of her esophagus we found a small hiatus hernia, illustrated in the last film. This is the one case in our series in which the clinical diagnosis had been made by the surgeon prior to roentgen exploration. Resection of the phrenic nerve has cured the patient of her dysphagia.

In conclusion:

The radiological investigation in the six cases which have been presented was of definite value in the diagnosis of diaphragmatic hernia.

Through accurate pre-operative diagnosis, it was possible to effect cures in all of these cases, and in a minimal period of time.

Bearing in mind the possibility of intestinal obstruction, it is essential that the diagnosis should be made before complications arise and assume major proportions.

The incidence of diaphragmatic hernia is probably much greater than we were at first led to believe. A typical shadows in the chest area should prompt the clinician and radiologist to compare notes, especially if the abnormality suggested by these shadows does not seem to correspond to the clinical entity. In doubtful cases there should be no hesitation in controlling the preliminary roentgenological findings by a barium study.

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Further details may be obtained by writing to: Dr. Maurice Lenz, President, New York Roentgen Society, 840 Park Avenue, New York 21.

TENTATIVE PROGRAM

Criteria for the Choice of Angiography versus Ventriculography in the Diagnosis of Brain Tumor	Ernst H. Wood
The Diagnosis and Treatment of Neuroblastoma	Robert S. Sherman, Robert F. Phillips and Robert Leaming
Growing Skeleton in Gargoylism; Early Lesions and their evolution	John Caffey
Massive Hemorrhage from the Upper Gastro-intestinal Tract	John A. Evans and Forbes Delany
The Roentgen Aspects of the Papilla of Vater	Maxwell H. Poppel, Harold G. Jacobson and Robert W. Smith
Abdominal Aortography	William Schlein
Congenital Arteriovenous Communications	Charles T. Dotter and Israel Steinberg
The Roentgen Diagnosis of Broncholithiasis	Coleman B. Rabin and Morton Ziskind
Fish-Bone Foreign Bodies of the Upper Esophagus and Pharynx: A Clinical and Experimental Study	Arnold L. Bachman
The Problem of Personnel Protection in Diagnostic Roentgenology	Lillian E. Jacobson, Joel J. Schwartzman and Saul Heiser
Some Rotation Therapy Technics Applicable to Standard Deep Therapy Machine	Morton M. Kligerman and Elaine Gilinson
The Effect of Single Doses of X-ray on Experimentally Induced Glioma	Martin G. Netsky and J. R. Freid
X-ray Therapy of Mongolism	Ira I. Kaplan
Segmental Resection and Radium Implantation in the Treatment of Carcinoma of the Bladder	John N. Robinson and Morton M. Kligerman
A Rapid Technic in Radiotherapy of Oral Carcinoma	Sidney Rubenfeld
Grid Therapy for Cancer of the Lung	Sidney M. Silverstone, William Harris and Charles Botstein
X-ray and Chemotherapy in the Management of Malignant Lymphomas	Vincent C. Collins and Alfred Gellhorn
Comparison of Tissue Doses for High Energy Radiation (1-70 MEV)	Carl B. Braestrup.

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